

**U.S.S.N. 09/482,682  
VON SEGGERN *et al.*  
AMENDMENT**

**IN THE CLAIMS:**

A listing of the claims, in accord with 37 CFR §1.121, is provided. The listing of claims replaces all prior such listings of claims. Claims 1, 2, 6-8, 13, 14, 16-20, 47, 69, 97-99, 102 and 103 are amended herein.

1. (Currently Amended) An isolated nucleic acid molecule comprising:  
a sequence of nucleotides encoding an adenovirus tripartite leader (TPL),  
wherein the TPL-encoding sequence of nucleotides comprises: (a) first and  
second different TPL exons, wherein the different TPL exons are from different  
adenoviruses, or in a non-native order or both or (b) first, second and third same  
or different TPL exons, wherein : ~~such that~~  
at least two are of the different TPL exons are from different adenoviruses, or in  
a non-native order or both; and

said TPL exons are selected from the group consisting of complete TPL  
exon 1, complete TPL exon 2 and complete TPL exon 3.

2. (Currently Amended) An isolated nucleic acid molecule, comprising:  
a sequence of nucleotides encoding an adenovirus tripartite leader (TPL) that  
comprises (a) first and second different TPL exons, wherein the different TPL  
exons are from different adenoviruses, or in a non-native order or both or (b)  
first, second and third same or different TPL exons, wherein at least two of the  
different TPL exons are from different adenoviruses, or in a non-native order or  
both, said TPL exons selected from the group consisting of complete TPL exon  
1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3, wherein  
the sequence of nucleotides encoding a TPL is operatively linked to an intron  
containing an RNA processing signal.

3. (Canceled)

4. (Previously Presented) The isolated nucleic acid molecule of claim  
2, wherein said intron is native adenovirus intron 1.

**U.S.S.N. 09/482,682**  
**VON SEGGERN *et al.***  
**AMENDMENT**

5. (Previously Presented) An isolated nucleic acid molecule, comprising a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein said TPL nucleotide sequence is set forth in SEQ ID NO: 32.

6. (Currently Amended) An isolated nucleic acid molecule, comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleotide sequence comprising (a) first and second different TPL exons, wherein the different TPL exons are from different adenoviruses, or in a non-native order or both or (b) first, second and third same or different TPL exons, wherein at least two of the different TPL exons are from different adenoviruses, or in a non-native order or both, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3 and further comprising a promoter and a sequence of nucleotides that encodes an adenoviral structural protein, operatively linked to said promoter and said TPL-encoding sequence of nucleotides.

7. (Currently Amended) The isolated nucleic acid molecule of ~~claim~~ claim 6, wherein said adenoviral structural protein is a fiber protein or a chimeric protein which includes an adenovirus fiber protein tail domain.

8. (Currently Amended) The isolated nucleic acid molecule of ~~claim~~ claim 7, wherein said chimeric protein comprises an Ad3 head domain and an Ad5 tail domain or an Ad5 head domain and an Ad3 tail domain.

9. (Previously Presented) The isolated nucleic acid molecule of claim 7, wherein said molecule is contained in a plasmid selected from the group consisting of plasmids pDV60, pDV67, pDV69, pDV80 and pDV90.

10. (Previously Presented) The isolated nucleic acid molecule of claim 9, wherein said molecule has a nucleotide sequence selected from the group consisting of sequences shown in SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 47, SEQ ID NO: 64 and SEQ ID NO: 65.

**U.S.S.N. 09/482,682**  
**VON SEGGERN *et al.***  
**AMENDMENT**

11. (Original) An adenovirus vector complementing plasmid comprising an isolated nucleic acid molecule according to claim 1.

12. (Previously Presented) An adenovirus vector packaging cell line, comprising:

i) a stably integrated nucleic acid molecule, comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleic sequence comprising (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3; and

ii) an operatively-linked promoter and a nucleic acid sequence that encodes an adenovirus structural protein,

wherein the sequence of nucleotides that encodes the TPL consists essentially of a first TPL exon operatively linked to a complete second TPL exon operatively linked to a complete third TPL exon.

13. (Currently Amended) The cell line of ~~claim 12~~claim 12, wherein said first TPL exon is a complete or partial ~~first TPL exon~~TPL exon 1.

14. (Currently Amended) The cell line of ~~claim 13~~claim 13, wherein said TPL molecule comprises complete TPL exon 1 having the nucleotide sequence of SEQ ID NO: 32 or partial TPL exon 1 having the nucleotide of SEQ ID NO: 26.

15. (Original) The cell line of claim 12 wherein said promoter is an inducible promoter.

16. (Currently Amended) The cell line of ~~claim 12~~claim 12, wherein said adenovirus structural protein is adenovirus fiber protein or a chimeric protein which includes an adenovirus fiber protein tail domain.

**U.S.S.N. 09/482,682**  
**VON SEGGERN *et al.***  
**AMENDMENT**

17. (Currently Amended) The cell line of ~~claim 16~~claim 16, wherein said chimeric protein comprises an Ad3 head domain and an Ad5 tail domain or an Ad5 head domain and an Ad3 tail domain.

18. (Currently Amended) The cell line of ~~claim 12~~claim 12, wherein said nucleic acid molecule is selected from the group consisting of plasmids pDV60, pDV67, pDV69, pDV80 and pDV90.

19. (Currently Amended) The cell line of ~~claim 18~~claim 18, wherein said nucleic acid molecule has a nucleotide sequence selected from the group consisting of sequences shown in SEQ ID NO: 43, SEQ ID NO: 44 and SEQ ID NO: 47.

20. (Currently Amended) The cell line of ~~claim 12~~claim 12, wherein said cell line is an epithelial cell line.

21. (Previously Presented) The cell line of claim 12, wherein said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome.

22. (Previously Presented) The cell line of claim 21, wherein said cell line expresses an adenovirus early protein gene and a fiber gene.

23. (Previously Presented) The cell line of claim 21, wherein deletion of a deficient viral gene is complemented by the expression of a gene under the control of an inducible promoter.

Claims 24-40 (Canceled)

41. (Previously presented) A method for producing an adenovirus particle comprising:

1) providing a packaging cell line wherein said packaging cell line comprises:

a) a stably integrated first nucleic acid molecule operatively linked to a promoter, and said first nucleic acid is operatively linked to a second nucleic acid molecule encoding an adenovirus structural protein, wherein said

**U.S.S.N. 09/482,682**  
**VON SEGGERN *et al.***  
**AMENDMENT**

first nucleic acid molecule comprises an adenovirus tripartite leader (TPL) nucleotide sequence operatively linked to an intron containing an RNA processing signal, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3 and

b) said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome, and

2) producing said adenovirus particle.

Claims 42-46 (Canceled)

47. (Currently Amended) The method of claim 41, wherein:

~~said nucleic acid molecule is a nucleic acid molecule comprising an adenovirus tripartite leader (TPL) nucleotide sequence, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3; and~~

~~said molecule further comprises a sequence encoding the adenovirus structural protein is adenovirus fiber protein.~~

Claims 48-68 (Canceled)

69. (Currently Amended) The packaging cell line of ~~claim 12~~claim 12, wherein said cell line is selected from the group consisting of 293, A549, W163, HeLa, Vero, 211, 211A and an epithelial ~~cell line~~cell line, wherein said cell line comprises said stably integrated nucleic acid molecule.

Claims 70-94 (Canceled)

95. (Original) A method for producing an adenovirus particle comprising:

**U.S.S.N. 09/482,682**  
**VON SEGGERN *et al.***  
**AMENDMENT**

1) providing a packaging cell line wherein said packaging cell line comprises:

a) a stably integrated first nucleic acid molecule operatively linked to a second nucleic acid molecule encoding an adenovirus structural protein, wherein said first nucleic acid molecule comprises an adenovirus tripartite leader (TPL) nucleotide sequence operatively linked to an intron containing an RNA processing signal, said TPL nucleotide sequence comprising (a) first and second different TPL exons or (b) first, second and third different TPL exons, said TPL exons selected from the group consisting of complete TPL exon 1, partial TPL exon 1, complete TPL exon 2 and complete TPL exon 3 and

b) said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome, and

2) producing said virus particle.

96. (Previously presented) A method for producing an adenovirus particle comprising:

1) providing a packaging cell line wherein said packaging cell line comprises:

a) a stably integrated nucleic acid molecule, comprising:

a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides comprises: (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, wherein said TPL exons are selected from the group consisting of complete TPL exon 1, complete TPL exon 2 and complete TPL exon 3; and

b) said cell line supports the production of a recombinant adenovirus vector genome by complementation of a deficient viral gene in said vector genome; and

**U.S.S.N. 09/482,682**  
**VON SEGGERN *et al.***  
**AMENDMENT**

2) producing said adenovirus particle.

97. (Currently Amended) A method for producing an adenovirus particle comprising:

1) providing a packaging cell line wherein said packaging cell line comprises: ~~[[the]]~~a stably integrated nucleic acid molecule, comprising:

a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides comprises: (a) first and second different TPL exons or (b) first, second and third same or different TPL exons, wherein said TPL exons are selected from the group consisting of complete TPL exon 1, complete TPL exon 2 and complete TPL exon 3, and a sequence of nucleotides encoding adenovirus fiber protein; and

2) producing an adenovirus particle.

98. (Currently Amended) The method of ~~claim 97~~claim 97, wherein said adenovirus particle comprises a genome encoding an exogenous protein.

99. (Currently Amended) The method of ~~claim 98~~claim 98, wherein said exogenous protein is selected from a group consisting of a tumor-suppressor protein, a biologically active fragment thereof that has tumor-suppressor activity, a suicide protein and a biologically active fragment thereof that has activity as a suicide protein.

100. (Original) The isolated nucleic acid molecule of claim 7, wherein said molecule is contained in plasmid pCLF.

101. (Previously Presented) The isolated nucleic acid molecule of claim 100 that has the sequence of nucleotides set forth in SEQ ID No. 8.

102. (Currently Amended) A plasmid having all of the identifying ~~characteristics~~characteristics of a plasmid deposited at the ATCC under accession no. 97737.

**U.S.S.N. 09/482,682**  
**VON SEGGERN *et al.***  
**AMENDMENT**

103. (Currently Amended) A plasmid having all of the identifying ~~characteristics~~characteristics of a plasmid deposited at the ATCC under accession no. PTA-1144, PTA-1145, PTA-1146, PTA-1147 or PTA-1148.